

Appl. No. : 09/574,819  
Filed : May 19, 2000

IN THE DRAWINGS:

**Please amend Figure 4.** In accordance with 37 CFR 1.121(3), attached please find a copy of original Figure 4 with red ink markings showing a proposed change to Figure 4 for which approval of the Examiner is requested. Additionally, attached please find a substitute drawing of Figure 4 for original drawing of Figure 4. Support for the amendment of Figure 4 is found throughout the specification, for example, at Figure 1, Example 4, and SEQ ID NO:15. No new matter is added. The amendment is to conform Figure 4 to the specification.

REMARKS

By this preliminary amendment, Applicant has canceled all pending claims, that is, Claims 1-26, prior to examination of this application, and, thus, for reasons unrelated to patentability. Claims 27-32 have been added. Thus, Claims 27-32 are presented for examination. Support for the amendment is found throughout the specification, for instance, at Example 4; see also Example 9. No new matter is added.

As indicated in the specification, partially purified extracts from newborn calf articular cartilage were found to induce cartilage and bone when subcutaneously implanted in rats. This activity showed characteristics of bone morphogenetic proteins (BMPs). Degenerate oligonucleotide primer sets derived from the highly conserved carboxyl-terminal region of the BMP family were designed and used in reverse transcription-polymerase chain reactions with poly(A)+ RNA from articular cartilage as template to determine which BMPs are produced by chondrocytes. Two members of the transforming growth factor- $\beta$  (TGF- $\beta$ ) superfamily were identified and designated cartilage -derived morphogenetic protein (CMDP-1) and -2 (CDMP-2). Their carboxyl-terminal TGF- $\beta$  domains are so similar that they define a new subfamily most closely related to the BMPs.

As specified in Example 4, results of protein alignments indicated that CDMP family members from several different species, including xenopus, human, chicken, bovine, and zebrafish, shared a common amino acid sequence motif. The consensus sequence deduced from the protein alignment is SEQ ID NO:15 (see also Fig. 4). Of the 31 amino acid positions deduced from the protein alignment, all but 5 were

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occupied by identical amino acid residues for all of the isolates. Such extraordinary amino acid sequence conservation is indicative of a functional domain. ("Those of ordinary skill in the art will appreciate that such extraordinary amino acid sequence conservation is indicative of a functional domain." At page 11, lines 9-10.) Neither USP 5,994,094 to Hotten et al. having a priority date of August 10, 1993 (hGDF5), USP 5,801,014 to Lee et al. having a priority date of January 12, 1993 (mGDF5), nor USP 5,770,444 to Lee et al. having a priority date of July 9, 1993 (mGDF6) describe a class of compounds identified (whether structurally or functionally) by the consensus sequence of SEQ ID NO:15.


#### CONCLUSION

In view of the foregoing, Applicant respectfully requests that the present amendment be entered prior to examination of this application. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

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